Remarks

Claims 9-23, 25-32, and 51-60 are pending in the subject application and Applicants have added new claims 61-81. Support for the new claims can be found throughout the subject specification and in the claims as originally filed (for example, paragraphs 444-449 of the corresponding published U.S. Patent Application US-2001-0041357-A1). Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 9-23, 25-32, and 51-81 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

As an initial matter, Applicants gratefully acknowledge the Examiner's withdrawal of the previous rejection under 35 U.S.C. § 112. Applicants further wish to thank the Examiner for the courtesy of the interview of September 10, 2004. As discussed during the course of the interview, Applicants respectfully submit that the references singly or in combination fail to establish a *prima facie* case of obviousness for the claimed invention as "at least one temperature regulated zone upon which a thermal transfer member acts and wherein said thermal transfer member cycles between at least two temperatures" is not taught or suggested by the references. As discussed in the interview, a "temperature regulated zone" is at least a portion of the pathway, through which a sample moves, that is acted upon by a "thermal transfer member" that cycles between at least two temperatures. An exemplary temperature regulated zone is illustrated in Figure 1 of the subject application. In this example, a single temperature zone is schematically illustrated in one embodiment of a microfluidics device according to the invention in which a microfluidic substrate 100 is mounted upon a metal bar 900 which transfers heat to temperature regulated zone in the microfluidic substrate. As is illustrated by the Figure, the temperature regulated zone is a portion of the substrate upon which the thermal transfer member acts (*e.g.*, heating or cooling the substrate as required by a particular protocol). As further discussed during the interview, Figure 2 illustrates a device with three metal bars 900, 901, and 902 and the microfluidic substrate 100 of Figure 1. In Figure 2, each of the metal bars provides thermal regulation (*i.e.*, heating or cooling) to a separate temperature regulated zone of the microfluidic substrate; thus, there would be three distinct temperature regulated zones in the illustrated portion of the microfluidic substrate of Figure 2.

Claims 9-12, 21, 22, 25-32, 51, 55, and 60 are rejected under 35 U.S.C. § 103(a) as obvious over Bach *et al.* (U.S. Patent No. 6,413,780). Applicants respectfully traverse the rejection. As the Patent Office is aware, to establish the *prima facie* obviousness of a claimed invention all the claim limitations must be taught or suggested by the prior art (*In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974)) and it is respectfully submitted that Bach *et al.* fail to teach or suggest all the limitations presented in the currently pending claims. The Office Action argues that Bach *et al.* teach, in Figure 3, a process path (11) that includes at least one temperature controller that keeps a portion of a first process path at a desired temperature and another temperature controller that keeps a second portion of the first process path at a second temperature. As discussed during the course of the interview, Applicants respectfully submit that Bach *et al.* fail to teach "temperature regulated zones" that cycle between at least two temperatures and upon which a thermal transfer member acts. As discussed above, a "temperature regulated zone" is a single section or region of a pathway that is acted upon by a thermal transfer member and which is cycled between at least two temperatures. This concept differs from the teachings of Bach *et al.* In the context of the subject invention, a single temperature regulated zone cycles between at least two different temperatures whereas the process path of Bach *et al.* is maintained at one temperature in a first temperature regulated zone (*i.e.*, a first portion of the process pathway) and a second temperature in a second temperature regulated zone (a second portion of the process pathway). Thus, Bach *et al.* fail to teach "temperature regulated zones" that are acted upon by separate and distinct thermal transfer members that cycle between at least two different temperatures. Additionally, it is respectfully submitted that Bach *et al.* fail to teach samples that are continuously moving through at least one temperature regulated zone that cycles between two different temperatures. Applicants respectfully submit that Bach *et al.* fail to teach each and every limitation of the independent claims of this application and, accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

In addition, claims 13-20, 23, 52, 53, and 56-58 are rejected under 35 U.S.C. § 103(a) as obvious over Bach *et al.* (U.S. Patent No. 6,413,780) as applied to claims 9-12, 21, 22, 25-32, 51, 55, and 60 above, and further in view of Burns *et al.* (U.S. Patent No. 6,271,021). The Office Action states that one of ordinary skill in the art

"would have been motivated to modify the device of Bach *et al.* by applying the micro scale devices as taught by Burns *et al.* because Burns *et al.* teach that the sample receiving region on a plate substrate having a plurality of wells, the wells have a film which is hydrophilic and the device is in micro scale and the advantage is that each sample droplet is separated from each other so that the risk of contamination is reduced (See column 9, lines 6-8). In addition, the microdroplet transport avoids the current inefficiencies in liquid handling and mixing of reagents (See column 20, lines 16-17). (Office Action at page 6, last paragraph).

Applicants respectfully traverse.

As noted *supra*, Bach *et al.* fail to teach at least "one temperature regulated zone" that is acted upon by a thermal transfer member to cycle the temperature regulated zone between at least two different temperatures and Bach *et al.* also fail to teach samples that are continuously moving through at least one temperature regulated zone that is cycling between at least two different temperatures. Applicants further submit that the teachings of Burns *et al.* fail to remedy the defects noted with respect to the teachings of Bach *et al.* Burns *et al.* do not teach samples that are continuously moving through at least one temperature regulated zone that is cycling between at least two different temperatures. As indicated in column 8, lines 25-40 and illustrated in Figure 1, samples are moved to a thermally controlled reaction chamber (C) where mixing and reactions occur; the samples do not continuously move through the thermally controlled reaction chamber, rather they are held in the chamber. The reference further indicates that products arising in the reaction chamber (C) are then moved to an electrophoresis module (D) where migration data is gathered by a detector (E). Thus, the reference fails to teach that the samples continuously move through a temperature regulated zone that is acted upon by a thermal transfer member that cycles the zone between at least two temperatures.

The Office Action further argues that one skilled in the art "would have been motivated to modify the device of Bach *et al.* by applying the micro scale devices as taught by Burns *et al.* because Burns *et al.* teach that the sample receiving region on a plate substrate having a plurality of wells, the wells have a film which is hydrophilic and the device is in micro scale and the advantage is

that each sample droplet is separated from each other so that the risk of contamination is reduced. In addition, the microdroplet transport avoids the current inefficiencies in liquid handling and mixing of reagents". Applicants respectfully submit that one skilled in the art would not have been so motivated for the following reasons.

As the Patent Office is aware, the Court of Customs and Patent Appeals has held that a case of *prima facie* obviousness cannot be found where the suggested combination of references would require a substantial reconstruction and redesign of the elements shown in the primary reference as well as a change in the basic principle under which the primary reference was designed to operate. *In re Ratti*, 270 F.2d 810, 813, 123 U.S.P.Q. 349, 352 (CCPA 1959). In the case of the instant invention, the modification of the device of Bach *et al.* by applying the micro scale devices as taught by Burns *et al.* would require substantial reconstruction and redesign of the elements shown in the primary reference. For example, it would be necessary to completely redesign and construct a substantially different process path because the microfluidic substrate of Burns *et al.* would not appear to be an element that could be substituted for the containers that are loaded into the process path by the container loader and transporter taught by Bach *et al.* (see column 7, lines 42-46). Indeed, it would not appear that the liquid handling components of the Bach *et al.* device could be used to deliver reagents or samples into microfluidic substrate of Burns *et al.* Additionally, the device of Bach *et al.* lacks a means for energizing the silicon-based devices taught by Burns *et al.* and the device of Bach *et al.* would require substantial redesign and reconstruction to provide contact pads to which the heating elements of the microfluidic device of Burns *et al.* must be attached to accomplish the movement of the sample and its reaction in the reaction chamber (see Burns *et al.*, paragraph bridging columns 12-13). Accordingly, it is respectfully submitted that the combination of Bach *et al.* and Burns *et al.* fails to raise a *prima facie* case of obviousness and reconsideration and withdrawal of the rejection is respectfully requested.

Claims 54 and 59 are rejected under 35 U.S.C. § 103(a) as obvious over Bach *et al.* (U.S. Patent No. 6,413,780) as applied to claims 9-12, 20-22, 25, 26, 28, 30-32, 51, 53, and 60 above, and further in view of Leatti *et al.* (presumed by Applicants to be Leavitt *et al.*, U.S. Patent No. 5,002,870). The Office Action argues that one skilled in the art would have been motivated to use the temperature cycler of Leavitt *et al.* in the method of Bach *et al.* in order to carry out biochemical

or chemical protocols because the temperature cycler of Leavitt *et al.* is for a total of 30 cycles and is convenient and because the teachings of Leavitt *et al.* provide a metal bar in fluid communication. Applicants respectfully traverse.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). In this regard, Applicants have reviewed the teachings of Leavitt *et al.* (column 17, lines 1-14) cited in the Office Action and have been unable to identify any mention of a metal bar in fluid communication with a plurality of water sources that provide water having said at least two temperatures. As is indicated in the paragraph 166 of the published application corresponding to this serial number,

> "... the metal bar 900 is in communication with a system of valves (such as electrovalves or pressure valves) 910 through a system of pipes 920. The pipes 920 may be made of any conventional materials such as, for example, those used in traditional plumbing. The valves 910 may be actuated either manually or by an automated system controlled by a central processing unit. The valves 910 are, in turn, in communication with a plurality (three in the embodiment of FIG. 1) of reservoirs 930 by another set of pipes 940. The reservoirs 930 may be large tanks capable of holding a fluid. Each reservoir 930 is capable of maintaining the temperature of a fluid therein at a specified level by, for example, any of well-known heating or refrigeration means. The fluid in each reservoir 930 is maintained at a different temperature. In the present embodiment, the three reservoirs are maintained at 55°C, 72°C and 94°C. However, the number and temperatures of the reservoirs may be any combination consistent with the protocol to be performed. Thus, the fluid in the reservoirs may heat or cool the temperature regulated zones to any desired temperature. For example, in some embodiments, a reservoir at 37°C may be present in addition to the reservoirs at 55°C, 72°C and 94°C. It will be appreciated that in embodiments employing more than one temperature regulated zone, each of the reservoirs may be in fluid communication with all of the temperature regulated zones or only with a portion of the temperature regulated zones in accordance with the protocol to be performed."

Thus, it is respectfully submitted that the combination of Bach *et al.* and Leavitt *et al.* fail to teach each and every limitation of the claimed invention and, accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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